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 NEWS  3  FEB 25   CA/CAPLUS - Russian Agency for Patents and Trademarks
                   (ROSPATENT) added to list of core patent offices covered
 NEWS  4  FEB 28   PATDPAFULL - New display fields provide for legal status
                   data from INPADOC
 NEWS  5  FEB 28   BABS - Current-awareness alerts (SDIs) available
 NEWS  6  FEB 28   MEDLINE/LMEDLINE reloaded
 NEWS  7  MAR 02   GBFULL: New full-text patent database on STN
 NEWS  8  MAR 03   REGISTRY/ZREGISTRY - Sequence annotations enhanced
 NEWS  9  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS  10 MAR 22   KOREAPAT now updated monthly; patent information enhanced
 NEWS  11 MAR 22   Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS  12 MAR 22   PATDPASPC - New patent database available
 NEWS  13 MAR 22   REGISTRY/ZREGISTRY enhanced with experimental property tags

 NEWS EXPRESS  JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005

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FILE 'CAPLUS' ENTERED AT 11:28:10 ON 28 MAR 2005
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=> s tnf (s) binding (s) protein (s) fusion (s) immunoglob?
L1 11 TNF (S) BINDING (S) PROTEIN (S) FUSION (S) IMMUNOGLOB?

=> dup rem l1
PROCESSING COMPLETED FOR L1
L2 11 DUP REM L1 (0 DUPLICATES REMOVED)

=> d l2 total ibib kwic

L2 ANSWER 1 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:272597 CAPLUS
DOCUMENT NUMBER: 141:5674
TITLE: Construction and production of concatameric human TNF receptor-immunoglobulin fusion proteins
AUTHOR(S): Yim, Su-Bin; Chung, Yong-Hoon
CORPORATE SOURCE: Department of Microbiology, College of Medicine, Hanyang University, Seoul, 133-791, S. Korea
SOURCE: Journal of Microbiology and Biotechnology (2004), 14(1), 81-89
CODEN: JOMBES; ISSN: 1017-7825
PUBLISHER: Korean Society for Microbiology and Biotechnology
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB Tumor necrosis factor-α (TNF-α) and lymphotoxin-α (LT-α, TNF-β) can initiate and perpetuate human diseases such as multiple sclerosis (MS), rheumatoid arthritis (RA), and insulin-dependent diabetes mellitus (IDDM). TNFs can be blocked by the use of soluble TNF receptors. However, since monomeric soluble receptors generally exhibit low affinity or function as agonists, the use of monomeric soluble receptors has been limited in the case of cytokines such as TNF-α, TNF-β, interleukin (IL)-1, IL-4, IL-6, and IL-13, which have adapted to a multi-component receptor system. For these reasons, very high-affinity inhibitors were created for the purpose of a TNFs antagonist to bind the TNFR and trigger cellular signal by using the multi-step polymerase chain reaction method. First, recombinant simple TNFR-Ig fusion proteins were constructed from the cDNA sequences encoding the extracellular domain of the human p55 TNFR (CD120a) and the human p75 TNFR (CD120b), which were linked to hinge and constant regions of human IgG1 heavy chain, resp. using complementary primers (CP) encoding the complementary sequences. Then, concatameric TNFR-Ig fusion proteins were constructed using recombinant PCR and a complementary primer base of recombinant simple TNFR-Ig fusion proteins. For high level expression of recombinant fusion proteins, Chinese hamster ovary (CHO) cells were used with a retroviral expression system. The transfected cells produced the simple concatameric TNFR-**Ig fusion proteins** capable of **binding TNF** and inactivating it. These soluble versions of simple concatameric TNFR-Ig fusion proteins gave rise to multiple forms such as simple dimers and concatameric homodimers. Simple TNFR-Ig fusion proteins were shown to have much more reduced TNF inhibitory activity than concatameric TNFR-Ig fusion proteins. Concatameric TNFR-Ig fusion proteins showed higher affinity than simple TNFR-Ig fusion proteins in a receptor inhibitor binding assay (RIBA). Addnl., concatameric TNFR-Ig fusion proteins were shown to have a progressive effect as a TNF inhibitor compared to the simple TNFR-Ig fusion proteins and conventional TNFR-Fc in cytotoxicity assays, and showed the same results for collagen induced arthritis (CIA) in mice in vivo.

L2 ANSWER 2 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 2003225159 EMBASE
TITLE: Infliximab but not etanercept induces apoptosis in lamina propria T-lymphocytes from patients with Crohn's disease.

AUTHOR: Van den Brande J.M.H.; Braat H.; Van den Brink G.R.; Versteeg H.H.; Bauer C.A.; Hoedemaeker I.; Van Montfrans C.; Hommes D.W.; Peppelenbosch M.P.; Van Deventer S.J.H.
CORPORATE SOURCE: Dr. J.M.H. Van den Brande, Lab. for Exp. Internal Medicine, Academic Medical Center, Meibergdreef 9, NL-1105 AZ Amsterdam, Netherlands. J.vandenbrande@amc.uva.nl
SOURCE: Gastroenterology, (1 Jul 2003) 124/7 (1774-1785).
Refs: 45
ISSN: 0016-5085 CODEN: GASTAB
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
037 Drug Literature Index
048 Gastroenterology
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Background & Aims: Steroid-refractory Crohn's disease responds to therapy with the chimeric anti-tumor necrosis factor (**TNF**)-α antibody infliximab. Etanercept, a recombinant **TNF** receptor/**immunoglobulin** G **fusion protein**, is highly effective in rheumatoid arthritis but not in Crohn's disease. Because both infliximab and etanercept are **TNF**-α-neutralizing drugs, we investigated the differences in **TNF**-α-neutralizing capacity and human lymphocyte **binding** and apoptosis-inducing capacity of both molecules. Methods: We used a nuclear factor KB reporter assay and a cytotoxicity bioassay to study **TNF**-α neutralization by infliximab and etanercept. Lymphocyte **binding** and apoptosis-inducing capacity was investigated using fluorescence-activated cell sorter analysis, annexin V staining, and cleaved caspase-3 immunoblotting using mixed lymphocyte. . . (PBL) from healthy volunteers and lamina propria T cells from patients with Crohn's disease. Results: Both infliximab and etanercept neutralized **TNF** -α effectively. Infliximab bound to activated PBL and lamina propria T cells, whereas **binding** of etanercept was equal to a nonspecific control antibody. Infliximab but not etanercept induced peripheral and lamina propria lymphocyte apoptosis. . . Infliximab activated caspase 3 in a time-dependent manner, whereas etanercept did not. Conclusions: Although both infliximab and etanercept showed powerful **TNF**-α neutralization, only infliximab was able to bind to PBL and lamina propria T cells and subsequently to induce apoptosis of activated lymphocytes. These data may provide a biological basis for the difference in efficacy of the 2 **TNF**-α-neutralizing drugs.

L2 ANSWER 3 OF 11 EMBASE
on STN
ACCESSION NUMBER: 2002075012 EMBASE
TITLE: Management of rheumatoid arthritis: Defining the role of etanercept.
AUTHOR: Keating G.M.; Jarvis B.
CORPORATE SOURCE: G.M. Keating, Adis International Limited, 41 Centorian Drive, Auckland 10, New Zealand. demail@adis.co.nz
SOURCE: Disease Management and Health Outcomes, (2002) 10/1 (17-39).
Refs: 141
ISSN: 1173-8790 CODEN: DMHOFV
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 030 Pharmacology
031 Arthritis and Rheumatism
036 Health Policy, Economics and Management
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . diagnosis of rheumatoid arthritis and that patients should be offered the most effective treatment available. Etanercept is a soluble dimeric **fusion protein** comprising two copies of the extracellular ligand-**binding** domain of the human p75 receptor for turnout necrosis factor-α (**TNF**.alpha.) linked to the

constant portion of human **immunoglobulin** G1. **TNF** α is thought to play an important role in the pathophysiology of rheumatoid arthritis; by **binding** the cytokine, etanercept blocks its biologic effects. In a 12-month double-blind, randomized study involving patients with early active rheumatoid arthritis,. . .

L2 ANSWER 4 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000067066 EMBASE
TITLE: Targeting cytokines to tumors to induce active antitumor immune responses by recombinant fusion proteins.
AUTHOR: Xiang J.
CORPORATE SOURCE: Dr. J. Xiang, Saskatoon Cancer Center, 20 Campus Drive, Saskatchewan, Sask. S7N 4H4, Canada
SOURCE: Human Antibodies, (1999) 9/1 (23-36).
Refs: 125
ISSN: 1093-2607 CODEN: HUANFP
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 016 Cancer
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English

AB Cytokines such as interleukin-2 (IL-2), gamma interferon (IFN-γ) and alpha tumor necrosis factor (**TNF**-α) are important mediators in immune responses against tumors. However, their therapeutic efficacy and clinical utilities in treatment of human malignancies. . . achieved at the tumor sites without resorting to patient-specific therapy. With the advance in biotechnology, two structurally disparate domains of **immunoglobulin** and cytokine can be brought together into one **fusion protein** molecule by **protein** engineering These engineered antibody-cytokine **fusion proteins** combine ihe unique targeting ability of tumor-specific antibodies with the multifunctional activity of cytokines. In general, there are two commonly engineered **fusion proteins**, the F(ab')2/cytokine expressed in mammalian cells and the single-cl;ain FV/cytokine expressed in Escherichia coli. Both the tumor-**binding** reactivity and the functional cytokine activity are maintained in most of **fusion proteins.** Therefore, these **fusion proteins** may be useful in targeting cytokine to tumors to stimulate immune destruction of tumors, while limiting severe toxic side-effects by the high dose of cytokine administration. Recent preclinical studies have shown that these **fusion proteins** are able to target cytokines to tumors expressing the tumor-associated antigen in vivo, and to inhibit both the primary and metastatic tumors in an immune competent animal model. Therefore. these recombinant **fusion proteins** may represent a new generation of novel immunotherapeutic reagents for the treatment of human malignant diseases.

L2 ANSWER 5 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:736687 CAPLUS
DOCUMENT NUMBER: 130:108996
TITLE: Minimal tumor necrosis factor receptor binding protein: optimum biological activity of a truncated p55 soluble tumor necrosis factor receptor-IgG fusion protein
AUTHOR(S): Corcoran, Anne E.; Scallon, Bernard J.; Trinh, Han; Chernajovsky, Yuti; Ghrayeb, John; Feldmann, Marc
CORPORATE SOURCE: Sunley Division, The Mathilda and Terence Kennedy Institute of Rheumatology, London, W6 8LW, UK
SOURCE: European Cytokine Network (1998), 9(3), 255-262
CODEN: ECYNEJ; ISSN: 1148-5493
PUBLISHER: John Libbey Eurotext
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

AB The authors have previously demonstrated, using expressed deletion constructs, that the 4th membrane proximal cysteine-rich repeat of the p55 TNF receptor (TNF-R) is not required for binding of tumor necrosis factor-α (TNF) or lymphotoxin-α (LT; tumor necrosis factor-β). The authors and others have also shown that the soluble p55 TNF-R, rendered dimeric by fusion to an IgG backbone is extremely effective at neutralizing the harmful effects of TNF overprodn., such as in toxic shock. Here the authors address the question of how the TNF binding properties of the truncated TNF-R comprising the 3 distal cysteine-rich repeats (Δ4 TNF-R), when fused with an IgG backbone, compare with those of the full length soluble receptor. The authors constructed several versions of the soluble Δ4 TNF-R, on a complete IgG heavy chain backbone and on an IgG lacking the CH1 (first constant region) domain. The constructs were expressed with an Ig or native TNF receptor leader sequence and altered or native N terminal sequence, to compare efficiency of expression. When compared with a full length, soluble receptor **Ig fusion protein**, the affinity of all for **TNF** was identical, as were their activities in in vitro **binding** and cytotoxicity assays. In vivo studies showed that the Δ4 and wild type fusion proteins afforded equivalent protection against LPS-induced lethality. However, the Δ4 proteins exhibited a lower affinity for LT, and reduced activity in LT binding and cytotoxicity assays. Thus, the truncated TNF receptor IgG fusion protein is as effective at neutralizing TNF activity as the full length soluble receptor fusion protein. Its lower affinity for LT may make it a more selective agent in blocking the action of TNF, while causing less interference with the action of LT. Also its smaller size may make it a more useful therapeutic agent as it may be less immunogenic than the full length receptor.

L2 ANSWER 6 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 97088580 EMBASE
DOCUMENT NUMBER: 1997088580
TITLE: Preclinical safety assessment of the recombinant TNF receptor-immunoglobulin fusion protein.
AUTHOR: Winter M.
CORPORATE SOURCE: M. Winter, Pharmaceutical Research, Preclinical Toxicology, F. Hoffmann-LaRoche Ltd., CH-4070 Basel, Switzerland
SOURCE: Clinical Immunology and Immunopathology, (1997) 83/1 (21-24).
Refs: 32
ISSN: 0090-1229 CODEN: CLIIAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
052 Toxicology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The tumor necrosis factor (**TNF**) is now recognized as one of the most pleiotropic mediators of host defense, immune regulation, and inflammatory response. Due to its broad spectrum of effects, **TNF** has been implicated as a key mediator in the pathogenesis of acute and chronic inflammatory conditions. The inhibition of bioactive **TNF** could therefore provide a substantial therapeutic benefit. One approach to a potent **TNF** antagonist is to use recombinant **protein** technology in the design of a molecule in which the heavy chain sequences of an **immunoglobulin** are fused with the ligand-**binding** region of the **TNF** receptor. This paper describes some aspects of the preclinical safety evaluation of the recombinant human **TNF** receptor-**immunoglobulin fusion protein** (TENEFUSE). Specific emphasis was placed on transgenic and gene-deleted mice models as central sources of information in the safety evaluation of this **TNF** antagonist.

L2 ANSWER 7 OF 11 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1996:304064 CAPLUS

DOCUMENT NUMBER: 124:340930
TITLE: Chimeric TNF-binding protein for treatment of autoimmune disease
INVENTOR(S): Booth, Robert Fredrick Geoffrey; Lesslauer, Werner
PATENT ASSIGNEE(S): F. Hoffmann-La Roche Ag, Switz.
SOURCE: PCT Int. Appl., 23 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9603141	A1	19960208	WO 1995-EP2788	19950715
W: AM, AU, BB, BG, BR, BY, CA, CN, CZ, EE, FI, GE, HU, IS, JP, KG, KP, KR, KZ, LK, LR, LT, LV, MD, MG, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TT, UA, US, UZ, VN				
RW: KE, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2195665	AA	19960208	CA 1995-2195665	19950715
AU 9531119	A1	19960222	AU 1995-31119	19950715
EP 772449	A1	19970514	EP 1995-926902	19950715
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LI, LU, NL, PT, SE				
CN 1154068	A	19970709	CN 1995-194299	19950715
JP 09508140	T2	19970819	JP 1995-505421	19950715
HU 76666	A2	19971028	HU 1997-180	19950715
BR 9508419	A	19971118	BR 1995-8419	19950715
CZ 283219	B6	19980218	CZ 1997-193	19950715
FI 9700247	A	19970121	FI 1997-247	19970121
NO 9700264	A	19970324	NO 1997-264	19970121

PRIORITY APPLN. INFO.: EP 1994-111455 A 19940722
WO 1995-EP2788 W 19950715

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(constant domains, **fusion** products with **TNF**-**binding proteins**; chimeric **TNF**-**binding protein** for treatment of autoimmune disease)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(A, constant domains, **fusion** products with **TNF**-**binding proteins**; chimeric **TNF**-**binding protein** for treatment of autoimmune disease)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(E, constant domains, **fusion** products with **TNF**-**binding proteins**; chimeric **TNF**-**binding protein** for treatment of autoimmune disease)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(G, constant domains, **fusion** products with **TNF**-**binding proteins**; chimeric **TNF**-**binding protein** for treatment of autoimmune disease)

IT **Immunoglobulins**
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(M, constant domains, **fusion** products with **TNF**-**binding proteins**; chimeric **TNF**-**binding protein** for treatment of autoimmune disease)

IT Glycoproteins, specific or class
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(**TNF**-BP (tumor necrosis factor-**binding protein**), **fusion** products with **Ig**; chimeric **TNF-binding protein** for treatment of autoimmune disease)

IT Lymphokine and cytokine receptors
Receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor necrosis factor, **fusion** products with **Ig**; chimeric **TNF-binding protein** for treatment of autoimmune disease)

IT Lymphokine and cytokine receptors
Receptors
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(tumor necrosis factor p55, **fusion** products, with **Ig** ; chimeric **TNF-binding protein** for treatment of autoimmune disease)

L2 ANSWER 8 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 96261492 EMBASE
DOCUMENT NUMBER: 1996261492
TITLE: OX40 is differentially expressed on activated rat and mouse T cells and is the sole receptor for the OX40 ligand.
AUTHOR: Al-Shamkhani A.; Birkeland M.L.; Puklavec M.; Brown M.H.; James W.; Barclay A.N.
CORPORATE SOURCE: MRC Cellular Immunology Unit, Sir William Dunn School of Pathology, University of Oxford,Oxford, United Kingdom
SOURCE: European Journal of Immunology, (1996) 26/8 (1695-1699). ISSN: 0014-2980 CODEN: EJIMAF
COUNTRY: Germany
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
AB OX40, a member of the tumor necrosis factor (**TNF**) receptor/nerve growth factor (NGF) receptor superfamily was first identified as a marker of activated rat CD4+ cells with the MRC. . . antibody (mAb). A ligand for OX40 (called OX40 ligand or OX40L) has recently been identified and has sequence similarity to **TNF**. Mouse OX40L-**immunoglobulin fusion protein** (OX40L-Ig) binds to activated mouse CD4+ and CD8+ cells suggesting that OX40 could have a differential pattern of expression on. . . rule out the presence of an alternative receptor on CD8+ cells that also binds the OX40L. We have compared the **binding** of the MRC OX40 mAb with that of OX40L-Ig to activated rat lymph node cells and show that both recognize the same **protein**, namely OX40 which is expressed on CD4+ and CD4+ CD8α+ cells, but not on CD4- CD8+ cells. We have raised a new mAb (MRC OX86) using recombinant mouse OX40 **protein** and show by two-color flow cytometry that mouse OX40 is expressed on CD4 and CD8 single-positive cells. In addition, the new MRC OX86 mAb, unlike the MRC OX40 mAb, did not block **binding** of the OX40L. We conclude that OX40 is differentially expressed on activated mouse and rat T cells and is the. . .

L2 ANSWER 9 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 95346130 EMBASE
DOCUMENT NUMBER: 1995346130
TITLE: Characterization of an anti-CD44 single-chain F(V) antibody that stimulates natural killer cell activity and induces TNFα release.

AUTHOR: Tan P.H.; Sandmaier B.M.; Stayton P.S.
CORPORATE SOURCE: Center for Bioengineering, University of Washington,Seattle, WA 98195, United States
SOURCE: Immunological Investigations, (1995) 24/6 (907-926). ISSN: 0882-0139 CODEN: IMINEJ
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . bodies. The scFv was refolded in a cystine/cysteine redox buffer and purified to homogeneity using anion exchange chromatography. The concentration-dependent **binding** isotherm of the S5 scFv was determined using both direct **binding** and competitive inhibition flow cytometry assays. S5 scFv effectively blocked FITC-conjugated MAb S5 **binding** to canine peripheral blood mononuclear cells (PBMC), possessing a mean EC50 (15 nM) equivalent to Fab' fragments of parental S5. . . . the parent Mab, stimulating the activation of natural killer (NK) cell activity and the release of tumor necrosis factor alpha (**TNF**-α) in canine PBMC. Like the parent antibody, scFv crossreacted with human CD44 as examined by direct **binding** to human PBMC in the flow cytometry assay as well as direct **binding** to human CD44 **immunoglobulin fusion protein** in an enzyme-linked immunosorbent assay (ELISA). It was also able to induce **TNF**.alpha. release in human PBMC. These result support previous work suggesting that monovalent **binding** is sufficient to generate the in vitro biological activity of S5 (1). The scFv S5 antibody will thus serve as. . .

L2 ANSWER 10 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
ACCESSION NUMBER: 94357254 EMBASE
DOCUMENT NUMBER: 1994357254
TITLE: Protective effect of 55- but not 75-kD soluble tumor necrosis factor receptor-immunoglobulin G fusion proteins in an animal model of gram-negative sepsis.
AUTHOR: Evans T.J.; Moyes D.; Carpenter A.; Martin R.; Loetscher H.; Lesslauer W.; Cohen J.
CORPORATE SOURCE: DIDB, Royal Postgraduate Medical School, Du Cane Road,London W12 0NN, United Kingdom
SOURCE: Journal of Experimental Medicine, (1994) 180/6 (2173-2179). ISSN: 0022-1007 CODEN: JEMEAV
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
006 Internal Medicine
026 Immunology, Serology and Transplantation
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
AB . . . aim of this study was to compare the ability of both a 55- and 75-kD soluble tumor necrosis factor receptor **immunoglobulin** G **fusion protein** (sTNFR-IgG) in protecting against death in a murine model of gram-negative sepsis. Pretreatment with 250 μg of the p75 construct delayed but did not avert death in this model, reducing peak bioactive **TNF**-α levels after infection from 76.4 ng ml-1 in control mice to 4.7 ng ml-1 in the treated group ($p < 0.05$, two-sample t test). However, these low levels of bioactive **TNF** -α persisted in the p75 **fusion protein**-treated animals compared with the controls and were sufficient to mediate delayed death. In contrast, pretreatment with 200 μg of the p55 sTNFR-IgG gave excellent protection against death with complete neutralization of circulating **TNF**. Studies of the **binding** of **TNF** -α with the soluble TNFR **fusion proteins** showed that the p75 **fusion** construct exchanges bound **TNF** -α about 50-100-fold faster than the p55 **fusion protein**. Thus, although both **fusion proteins**

in equilibrium bind **TNF**- α with high affinity, the **TNF**-α p55 **fusion protein** complex is kinetically more stable than the p75 **fusion** construct, which thus acts as a **TNF** carrier. The persistent release of **TNF**-α from the p75 **fusion** construct limits its therapeutic effect in this model of sepsis.

L2 ANSWER 11 OF 11 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 94341444 EMBASE
DOCUMENT NUMBER: 1994341444
TITLE: Characterization of a CD6 ligand(s) expressed on human- and murine-derived cell lines and murine lymphoid tissues.
AUTHOR: Wee S.F.; Wang W.-C.; Farr A.G.; Nelson A.J.; Patel D.D.; Haynes B.F.; Linsley P.S.; Aruffo A.
CORPORATE SOURCE: Immunex Corp.,Seattle, WA 98101, United States
SOURCE: Cellular Immunology, (1994) 158/2 (353-364).
ISSN: 0008-8749 CODEN: CLIMB8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB . . . purpose of this study was to identify cell lines and tissues which express CD6 ligand(s), determine the requirements for CD6 **binding**, and biochemically characterize the putative CD6 ligand(s). **Binding** studies with a CD6 **immunoglobulin fusion protein**, CD6-Rg, allowed the identification of a number of human cell lines which express a CD6 ligand(s). The **binding** to these cell lines was trypsin sensitive, in part required divalent cations, was blocked by an anti-CD6 mAb, and could be downregulated by tumor necrosis factor α (**TNF**.alpha.), interleukin-1β (IL-1β) and interferon-γ (IFN-γ). Among the cell lines tested, the human breast carcinoma-derived cell line HBL-100 expressed the highest. . .

=> log y

COST IN U.S. DOLLARS	SINCE FILE ENTRY	TOTAL SESSION
FULL ESTIMATED COST	41.97	42.18

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE ENTRY	TOTAL SESSION
CA SUBSCRIBER PRICE	-1.46	-1.46

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Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1	153	tnf same fusion same immunoglob$8 same bind$8	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/28 11:43
S1	2	"5981701".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2005/03/28 11:42
S2	2	"5811261".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2003/10/14 13:25
S3	2	"5695953".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/07/08 12:17
S4	2	"5610279".pn.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	ON	2004/07/08 12:17